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Effective connectivity during processing of facial affect: Evidence for multiple parallel pathways

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Title: Effective connectivity during processing of facial affect: evidence for multiple parallel pathways

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Abstract

The perception of facial affect engages a distributed cortical network. We used functional magnetic resonance imaging and dynamic causal modelling to characterise effective connectivity during explicit (conscious) categorisation of affective stimuli in the human brain. Specifically, we (i) examined the modulation of connectivity from posterior regions of the face processing network to the lateral ventral prefrontal cortex (VPFC) during affective categorisation and (ii) tested for a potential role of the amygdala (AMG) in mediating this modulation. We found that explicit processing of facial affect led to prominent modulation (increase) in the effective connectivity from the inferior occipital gyrus (IOG) to the VPFC, while there was less evidence for modulation of the afferent connections from fusiform gyrus and AMG to VPFC. More specifically, the forward connection from IOG to the VPFC exhibited a selective increase under anger (as opposed to fear or sadness). Furthermore, Bayesian model comparison suggested that the modulation of afferent connections to the VPFC was mediated directly by facial affect, as opposed to an indirect modulation mediated by the AMG. Our results thus suggest that affective information is conveyed to the VPFC along multiple parallel pathways and AMG activity is not a sufficient account for the gating of information transfer to the VPFC during explicit emotional processing.

Introduction

Emotions are core aspects of mental life. Several meta-analyses (Phan et al., 2002; Murphy et al., 2003; Fusar-Poli et al., 2009; Vytal and Hammann, 2010) have attempted to formulate models of the neural circuitry underlying emotional processing. The majority of studies included in these meta-analyses use facial affect as a probe for emotional processing. Facial affect processing involves a number of functionally and anatomically connected cortical and subcortical brain structures, including the inferior occipital gyrus (IOG) (Haxby et al., 2000), the fusiform gyrus (FG) (Haxby et al., 2002; Hoffman and Haxby, 2000), the amygdala (AMG) and the ventral prefrontal cortex (VPFC) (Adolphs, 2002; Fairhall and Ishai, 2007). Within this network, the AMG is thought to play a key role in the rapid detection of facial affect and in biasing behavioural responses accordingly (LeDoux, 1998; Rolls, 1999). In contrast, the VPFC is thought to be involved in a more detailed evaluation of emotional stimuli and their contextual significance (Iidaka et al., 2001; Ochsner and Gross, 2005; Quick and Beer, 2006). Crucially, the processing of facial features in this network is context sensitive. The AMG, may be more engaged when facial expressions are processed outside the focus of attention (implicit processing), or when attention is directed towards non-affective cues (e.g. gender or facial features) (Critchley et al., 2000; Hariri et al., 2003). In contrast, when subjects are engaged in facial affect labelling (explicit processing), AMG activation may be reduced (Critchley et al., 2000; Hariri et al., 2000; Dyck et al., 2010). In addition, within visual cortices responses to emotional faces are generally enhanced (Vuilleumier and Driver, 2007). This phenomenon has been attributed to modulation of early visual processing by

prefrontal regions via mechanisms of selective attention (Armory and Dolan, 2002); although some models highlight the role of the AMG as the source of signal amplification both for sensory processing and prefrontal engagement (Anderson and Phelps 2001; Pessoa et al., 2002). Given such conflicting accounts, we wanted to characterise the functional interrelationships among the structures involved in facial affect processing and infer the direction of effects mediated by critical pathways in the network.

In this study, we combined conventional Statistical Parametric Mapping (SPM) with dynamic causal modelling (DCM) of functional magnetic resonance imaging (fMRI) data (Friston et al., 2003) to investigate effective connectivity within the face perception network and its modulation by affect in 40 healthy adults performing a face affect categorisation task. The aims of the study were twofold. First, we hypothesized that the explicit processing or categorisation of affective stimuli would increase the connectivity from posterior regions of the face processing network to the VPFC. Second, we investigated the role of the AMG during conscious processing of facial affect by testing the hypothesis implied by previous work (Anderson and Phelps, 2001; Pessoa et al., 2002) that AMG “gates” prefrontal connectivity during affect processing.

Materials and Methods

Subjects

Forty healthy adults (Table 1) were recruited via advertisement in the local press and were included if they (i) were aged 18–65 years, (ii) had no personal lifetime history of mental health problems, substance use, head injury or medical disorders (as assessed following personal interview with trained psychiatrists using the Structured Interview for DSM-IV-TR Axis I Disorders, non-patient edition: First et al., 2002), (iii) did not take any prescribed medication and (iv) were of self-reported British white ancestry. An estimate of current intellectual function (IQ) was obtained using the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Wechsler, 1981). Educational level was scored on a 5-point scale, where 1 indicated no formal qualifications and 5 indicated postgraduate-level qualifications.

The study was approved by the Ethics Committee of the Institute of Psychiatry and the South London and Maudsley National Health Service Trust. Written informed consent was obtained from all subjects.

Experimental design

We studied three negative emotions (anger, fear and sadness) in three separate event-related facial affect recognition fMRI experiments conducted in a single acquisition session in a randomised order. Each experiment lasted for 5 minutes. In

each experiment, ten different facial identities (six female, four male; www.paulekman.com) were presented; depending on the experiment, they either depicted anger, fear or sadness or a neutral facial expression. The facial identities were manipulated by computer software to depict 150% intensity of the emotion. The 150% level of intensity was chosen to minimize ambiguity and uncertainty about the nature of the stimuli (Phillips et al. 1997; Calder et al., 1997). Faces were presented in alternation with a fixation cross in a pseudo-random order. The neutral faces and affective faces were each displayed for 2 s and repeated 20 times giving a total of 60 images (Figure 1). The inter-stimulus interval followed a Poisson distribution and was varied between 3 s and 9 s (mean interval 5 s). Participants were instructed to press the right or left button with their dominant hand on a MRI-compatible response box to indicate whether the face was emotional or neutral. Subjects were familiarised with the task off-line, one hour prior to the scan. Response time and accuracy data were collected.

Image acquisition

Gradient echo planar MR images were acquired using a 1.5 T GE Sigma MR system (General Electric, Milwaukee, WI, USA) fitted with 40 mT/m highspeed gradients. Foam padding and a forehead strap was used to limit head motion, and a quadrature birdcage head coil was used for radio frequency (RF) transmission and reception. In each of the 16 non-contiguous planes parallel to the inter-commissural (AC–PC) plane, T2*-weighted MR images reporting blood-oxygenation level-dependent (BOLD) contrast were acquired (TR=2000 ms, TE=40 ms, flip angle=70°, slice

thickness=7 mm, slice skip=0.7 mm, matrix size=64*64, voxel dimensions=3.75x3.75x7.7 mm). For each participant 3 x 150 fMRI images were acquired.

During the same session, a high-resolution T1 weighted structural image was acquired in the axial plane (inversion recovery prepared, spoiled gradient-echo sequence; TR=18 ms, TE=5.1 ms, TI= 450 ms, flip angle=20°, slice thickness=1.5 mm, matrix size=256*192, FOV=240x180 mm, voxel dimensions=0.9375x0.9375x1.5 mm, number of excitations=1) for subsequent co-registration.

Image processing

Pre-processing

For image pre-processing and GLM analysis we used the SPM8 software package (Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, London, <http://www.fil.ion.ucl.ac.uk>); for effective connectivity analyses, DCM8 was employed. Pre-processed images were realigned to correct for movement and normalized into MNI space using each subject's structural MRI image. The spatially normalised data were smoothed with an isotropic Gaussian filter (8 mm full width half maximum) to compensate for normal variation in structural and functional anatomy across subjects.

First level (within-subject) analysis

For each subject, the data from the three experiments (emotions) were concatenated and modelled with a general linear (convolution) model, with additional regressors representing potential confounds (see below). Vectors of onset representing the correctly identified angry, fearful and sad faces and correctly identified neutral faces were convolved with a canonical haemodynamic response function. Serial correlations were removed using an AR(1) model and a high pass filter (128 s) was applied to remove low-frequency noise. An explicit mask was used to ensure only voxels within the brain were included in the analysis. Six movement parameters were also entered as nuisance covariates. Additionally, the means of the 3 sessions were modelled as well as the transition at the end of each session. Contrast images of brain activations associated with correct categorisation of emotional faces (anger, fear and sad) compared to neutral faces were produced for each participant.

Second level (between-subject) analysis

Group-level analyses were based on random-effects analyses of the single-subject contrast images using the summary statistic approach. For facial affect, one-sample t-tests were used to investigate the main effect of task (correctly identified emotional faces > correctly identified neutral faces). The statistical threshold was adjusted to provide a family-wise error rate (FWE) of $p=0.05$ (based on the spatial extent of clusters of voxels thresholded $p < 0.001$), corrected for multiple

comparisons across the whole brain. For all analyses, results are reported in the Montreal Neurological Institute (MNI) coordinate system.

Volumes of interest

We selected a priori volumes of interest (VOIs) within a right-hemispheric network of regions implicated in face processing and its modulation by affect, following previous work (Fairhall and Ishai, 2007). These VOIs comprised the inferior occipital gyrus (IOG; $x = 44$, $y = -78$, $z = -6$), the fusiform gyrus (FG; $x = 24$, $y = -56$, $z = -12$), the amygdala (AMG; $x = 20$, $y = -2$, $z = -16$) and the inferior frontal gyrus within the ventrolateral PFC (VPFC; $x = 52$, $y = 20$, $z = -6$). The coordinates for the visual regions, IOG and FG, were based on the group maxima from the contrast of all faces (minus crosshair), while for the “emotional” regions, AMG and IFG, the coordinates were specified from the contrast of emotional minus neutral faces. For each subject we chose subject-specific maxima (in the appropriate SPM) in these regions that were (i) within 4 mm from the group maxima and (ii) within the same anatomical area, as defined by the PickAtlas toolbox (Maldjian et al., 2003). Regional time series were summarised with the first eigenvariate of all activated (at $p < 0.01$) voxels within 5 mm of the subject-specific maxima.

Dynamic causal modelling

Dynamic Causal Modeling (DCM) (Friston et al., 2003) is a Bayesian model comparison procedure used to infer effective connectivity between brain regions.

DCM estimates directed interactions within neural systems. Crucially, it models these interactions at the neuronal level and distinguishes between endogenous coupling and context-specific coupling, while accounting for the effects of experimentally controlled network perturbations (cf. stimulus-locked coupling) (Friston et al. 2003; Penny et al. 2004).

A four-area DCM was specified for all subjects with bidirectional endogenous connection between all regions (IOG, FG, AMG, VPFC) and the main effect of “all faces” as the driving input entering the IOG, the visual input region of our model. This base model (Figure 2a) was then elaborated systematically to produce 7 alternative variants. These variations were guided by our primary aim to define the role of the VPFC in facial affect recognition and the modulation of afferent connections to VPFC by affect (*anger, fear and sadness*). Figure 2b shows the 7 variants of four-area models which include all possible combinations of how facial affect could modulate the forward connections to the VPFC. Note that while these figures show, for clarity, a single modulatory term labelled “Facial Affect”, the models contained distinct modulatory inputs for anger, fear and sadness, respectively, allowing us to test the modulatory effects of these emotions (on connectivity) separately.

An additional (bilinear) model was constructed, where affective stimuli directly entered AMG, to test if affective information transfer to the VPFC is mediated by the AMG (Figure 2b, Model 8). Furthermore, three additional non-linear models were constructed which allowed for multiplicative interactions of postsynaptic inputs

(Stephan et al., 2008). In these models affective stimuli drove AMG activity directly, which then modulated the forward connections (from IOG and/or FG) to the VPFC (Figure 2c, Models 9, 10, 11). These non-linear models replace the direct modulatory effect of experimentally defined facial affect with a vicarious physiological influence that is mediated by synaptic connections from the AMG. All 11 models (Figure 2) were constructed, fitted and compared for each of the 40 subjects in this study.

Note that we limited our model comparisons to the right hemisphere, investigating the modulation of forward (afferent) connections to VPFC. This was motivated by the study by Fairhall & Ishai (2007) who highlighted the predominance of the right hemisphere in the processing of emotional faces. Additionally we assumed that visual input entered the IOG (as the lowest visual area). These constraints made it possible to define a relatively small model space (11 models per subject), in which we systematically investigated which of the forward connections was subject to modulation by facial affect and whether this modulation was best modelled by the direct effect of facial affect (bilinear models) or could be explained indirectly via by AMG modulation (non-linear models) (Figure 2).

Model Comparison

Model comparison was implemented using random-effects (RFX) Bayesian Model Selection (BMS) in DCM8 to compute exceedance and posterior probabilities at the group level (Stephan et al., 2009). The exceedance probability of a given model denotes the probability that this model is more likely than any other model tested,

given the data. Additionally we made inferences about families of models (Penny et al., 2010; Stephan et al., 2010). Specifically our models were divided into a bilinear (Models 1-8) and a non-linear family (Models 9-11) in order to test whether or not AMG activity could provide a sufficient account for the modulation of connections to VPFC. All models were included in the BMS procedure, both when comparing individual models and model families. Finally, to summarise the strength of effective connectivity and its modulation quantitatively, we used random effects Bayesian Model Averaging (BMA) to obtain average connectivity estimates (weighted by their posterior model probability) across all models and all subjects (Penny et al., 2010).

Correlation with behavioural measures

To examine correlations between effective connectivity and behaviour, we applied BMA on a subject-by-subject basis across all models and then extracted the resulting posterior means for each subject. These were entered into a subsequent correlation analysis with behavioural measures (accuracy and response time) with Bonferroni correction for multiple comparisons.

Finally, we subjected the subject-specific BMA parameter estimates to one-sample tests to assess their significance in a classical sense (i.e., consistency across subjects). Behavioural and demographic data and parameter estimates were analyzed using SPSS 15 (SPSS Inc, Chicago, IL, USA) using one-sample t-tests, or appropriate non-parametric tests (one-sample Kolmogorov-Smirnov test) when data were not normally distributed based on the Kolmogorov-Smirnov criterion, with $\alpha=0.05$.

Since we tested 25 parameters of interest (i.e., all endogenous connections and all bilinear and non-linear modulations), we applied Bonferroni-correction for multiple comparisons, resulting in an adjusted threshold of $\alpha=0.002$.

Results

Behavioural data

Subjects identified all facial affects with a high rate of accuracy as seen in Table 1.

SPM analysis

In accordance with previous meta-analytic studies (Phan et al., 2002; Murphy et al., 2003; Fusar-Poli et al., 2009; Vytal and Hammann, 2010), robust activation in response to emotional faces (relative to neutral faces) was evident in the visual association cortices, the temporal gyrus as well as in frontal areas. Details of the regional maxima are provided in Figure 3 and 4 and Table 2.

DCM analysis

Comparing the individuals models

Model 1 outperformed all other models with an exceedance probability of 38% (Figure 5). This optimal Model 1 contained reciprocal endogenous connections between all four areas (IOG, FG, AMG, VPFC), with affect only modulating the

forward connection from the IOG to the VPFC. Model 3 was the second best model with exceedance probability of 20%. In Model 3, affect modulated the forward connection from AMG to the VPFC.

Comparing the bilinear and non-linear families

In a next step, we applied random effects BMS at the family level to clarify whether or not the AMG played a sufficient role in modulating forward connections to VPFC during processing of facial affect. Comparison between the bilinear (Models 1-8) and non-linear families (Models 9-11) showed that the bilinear family was superior to the non-linear family with an exceedance probability of 100%. This suggests that the AMG alone does not provide a sufficient account for the gating of transfer of facial affect to VPFC. Note that Bayesian model comparison eschews null results. In other words, we can be nearly 100% confident that the (direct) modulatory effects of facial affect provide a better model of empirical responses than a model in which the equivalent modulation is mediated (indirectly) by the AMG.

Bayesian Model Averaging

The results from the BMA across all subjects and across all eleven models are shown in Table 3. The implementation of RFX BMA in SPM8 employs an Occam's window for computational efficiency (Penny et al. 2010), excluding from the average those models whose probability ratio (compared to the best model) is below 0.05. In our case this applied to the three non-linear models (models 9-11).

The BMA results highlight the importance of the efferent connections from the IOG to FG, AMY, and VPFC in the network. When BMA parameter estimates of the endogenous connections originating from IOG were tested for consistency across subjects with classical t-tests, they were found to be highly significant, even when correcting for multiple comparisons. Furthermore, the IOG→VPFC connection was strongly and significantly modulated by anger ($p < 0.001$; Table 3). It also showed a substantial modulation by fear ($p < 0.017$) although this did not quite survive Bonferroni correction ($\alpha = 0.002$). By contrast, sadness did not change this connection significantly ($p = 0.076$). Altogether, these results emphasized the importance of this direct connection to VPFC for the categorisation of facial affect (Figure 6).

Behavioural Correlations

We performed correlations between response time and accuracy for angry, fearful and sad faces, with the modulatory parameters from BMA on a subject-by-subject basis over models. Mean response time to angry faces showed a significant negative correlation with *anger* modulation of the forward connections from FG ($r = -0.336$, $p = 0.034$) and from AMG to the VPFC ($r = -0.337$, $p = 0.034$). Mean response time to fearful faces showed a significant positive correlation for *fear* modulation on the forward connection from the IOG to the VPFC ($r = 0.376$, $p = 0.017$). However, these correlations did not survive Bonferroni correction for multiple tests.

Discussion

In this study we assessed effective connectivity during facial affect processing using DCM as an established method for inferring effective connectivity from fMRI data (Stephan et al., 2010). Our aim was to examine the modulation of connectivity between posterior regions of the face processing network and the ventral prefrontal cortex (VPFC) during affect categorisation and to evaluate the role of the amygdala (AMG) in mediating this modulation. There are three key findings from our study. Firstly, we confirmed our hypothesis that facial affect significantly increased effective connectivity between posterior regions of the face network and the VPFC. Our data were best explained by a model in which facial affect modulated the connection from the inferior occipital gyrus (IOG) to the VPFC. Secondly, our results suggest that affect may modulate connections to the VPFC above and beyond any putative modulation by the AMG. This implies that the AMG is not necessarily involved in “gating” prefrontal connectivity during explicit affective processing. Thirdly, the effective connectivity between the IOG and VPFC showed evidence for differential modulation according to valence, with the strongest modulation observed for anger.

These findings are timely in view of the current revaluation of existing models of affective stimuli processing in the brain (Pessoa and Adolphs, 2010). Our results contribute to this debate by highlighting the role of the prefrontal cortex during affective processing and by questioning the prevailing “amygdalocentric” model of affective processing (LeDoux 1996; Davis and Whalen 2001).

Across all subjects, our modeling results suggest that the VPFC receives information directly from regions within the face network. Crucially, however, it was the coupling from the IOG to the VPFC that emerged as the most significant effective connection within this network, which was further enhanced during the processing of facial affect. A large body of literature has established that attention enhances neural responses primarily within extrastriate visual cortices (Moran and Desimone 1985; Bufallo et al., 2010). A similar enhancement has also been noted in response to emotional valence in general (Lane et al., 1999) and also during presentation of emotional, particularly negative (Vuilleumier et al., 2004), facial expressions compared to neutral ones (e.g. Critchley et al., 2000; Vuilleumier et al., 2001; Winston et al., 2003). Electrical recordings have shown that during attentive viewing, prefrontal and visual cortices show increased gamma frequency synchrony suggestive of greater functional coupling between these regions (Gregoriou et al., 2009). Our results therefore add support to the notion of increased coupling between prefrontal and visual cortical regions during visual attention and suggest that such coupling may be further increased when attention is directed to the emotional valence of the stimuli.

Research in affective neuroscience has traditionally emphasized the role of the AMG in emotional processing. The AMG is considered a core component of a subcortical pathway for the rapid detection of emotions during visual processing (LeDoux, 1998; Morris, 1999; Rolls, 1999) and is thought to influence behaviour through the modulation of PFC activity (Miller and Cohen, 2001). There are innumerable examples from multiple lines of research showing that the AMG modulates activity

in the ventral visual pathway in response to emotional signals (e.g. Sugase et al., 1999), including facial expressions of affect (e.g. Pessoa et al., 2002; Vytal and Hamann, 2010). Although the contribution of the AMG to emotional processing is indisputable, our results, together with those of others (Tsuchiya et al., 2009; Piech et al., 2010; Pessoa and Adolphs, 2010), suggest that the amygdalocentric model of affect processing overlooks the significant contribution of other brain regions and the complexity of their interactions. Our modeling results imply that the VPFC receives information about facial affect directly from three distinct brain regions, the IOG, the fusiform gyrus (FG) and the AMG, and that AMG modulation of the connections from either the FG or the IOG to the VPFC was not a complete or sufficient explanation for changes in coupling. While the results of the present study do not disclose the sources of this modulation, they imply that AMG activity does not necessarily 'gate' the transfer of facial affect information towards the VPFC. Instead, they support a model in which affective information from visual stimuli proceeds simultaneously along parallel 'channels', creating 'multiple waves' of activation across the face processing network (Pessoa and Adolphs, 2010). One may speculate that the emotional modulation of these 'channels' may have arisen from multiple, and possibly diffuse, sources; these, however, were not visible in the statistical parametric maps of our present fMRI study. Finally, the implausibility of an amygdalocentric explanation of our data, as indicated by our model comparisons, may be due to the fact that the effective connectivity (and its affect-sensitive changes) assessed by our paradigm mediated the explicit or conscious processing of affective stimuli. This contrasts with the implicit and automatic processes normally associated with AMG processing.

The inclusion of facial identities with three distinct negative affects allowed us to explore the effect of valence on effective connectivity within the face processing network. Our results suggest that *anger* showed the most potent modulation of the coupling from the IOG to the VPFC. Anger is considered particularly salient compared to other emotions, as it signals the need for immediate action in response to perceived threat. The VPFC is thought to exert a regulatory role in the expression of anger as damage to the VPFC can increase violent and aggressive behaviours (Grafman et al., 1996; Damasio et al., 1994). Our findings complement results from a recent meta-analytic review of the discrete neural correlates of basic emotions, which suggested that the rapid engagement of the VPFC during exposure to anger stimuli may serve to avert potential overreaction, such as unrestrained rage (Vytal and Hamann, 2010).

Finally, concerning the AMG, our results based on Bayesian model averaging suggest that the differential responses to affective vs. neutral faces in the AMG arise via two afferent connections (Table 3), i.e., the IOG→AMG connection ($p < 0.0001$) and the VPFC→AMG connection ($p < 0.018$, not quite surviving Bonferroni correction at $\alpha = 0.002$).

Our study focused on effective connectivity within the face processing network during attentive viewing and categorisation of facial affect. Since the ensuing estimates of effective connectivity are context and paradigm-dependent, further studies are required to explore the functional architecture of the facial affect processing network during tasks that make additional cognitive demands involving

induction or suppression of emotional responses. Our findings have significant implications for pathophysiological models of affective dysfunction in psychiatric disorders, particularly mood disorders where current amygdalocentric approaches may need to be re-evaluated.

In summary, our analyses have identified that during the processing of facial affect effective connectivity to the VPFC is increased not only from the AMG but also with other regions in the ventral visual stream, namely the FG and IOG. AMG modulation of this coupling does not appear to be a sufficient account of affect dependent changes during explicit (conscious) processing. Finally, the functional coupling of the IOG to the VPFC plays a major role in the processing of facial affect and suggests a greater contribution of visual cortical – prefrontal pathways to affect processing than previously considered.

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Figure Legends

Figure 1. The design of one facial affect recognition experiment is depicted (note that this example uses fear expressions). Subjects viewed pseudo-randomised neutral expressions and affect-laden (angry or fearful or sad) facial expressions at 150% intensity, during each of three separate experiments. Subjects judged the presence or absence of the facial emotion and pressed the corresponding button on an MRI-compatible response box.

Figure 2. Model specification: The sources comprising the models were: IOG: inferior occipital gyrus; FG: fusiform gyrus; AMG: amygdala; VPFC: ventral prefrontal cortex. Schematically, the modulations are represented as one Facial Affect (•), but correspond to the three distinct modulations: angry faces (Anger), fear faces (Fear) and sad faces (Sadness). **a.** A four-area DCM was specified with bidirectional endogenous connections between all regions (IOG, FG, AMG, VPFC) and with driving input of 'all faces' into the IOG. **b.** The eight models, which constitute the **bilinear** family. **c.** The three models, which constitute the **non-linear** family. In these models, the effect of facial affect is mediated vicariously through the AMG: Facial Affect directly enters the AMG. The AMG directly modulates the forward connections to the VPFC.

Figure 3. Image showing task-related brain activation in the group (N=40) during explicit (conscious) categorisation of affective facial stimuli (FWE cluster-level corrected at $p < 0.05$ across the whole brain, with voxel-level threshold of $p < 0.001$).

Figure 4. The graphs show the mean and the standard error of mean of the GLM parameter estimates from the subject-specific maxima for all four conditions (neutral, anger, fear, sad) and for the four areas included in the models for dynamic causal modelling (**IOG**: inferior occipital gyrus; **FG**: fusiform gyrus; **AMG**: amygdale; **VPFC**: ventral prefrontal cortex).

Figure 5. Expected Probability and Exceedance Probability for the eleven models specified (N=40).

Figure 6. Alterations in effective connectivity within the face processing network across all subjects (N=40), established by Bayesian model averaging across all models considered. Thick grey arrows indicate significant endogenous connections ($p < 0.0001$), the thick black arrow indicates a significant endogenous connection, significantly modulated by anger ($p = 0.001$). Dashed arrows indicate backwards connections and solid black arrows indicate bidirectional connections.

Table 1. Demographic data and task information: Mean (standard deviation)

	Group (n=40)
Gender (male:female)	20:20
Age in years	31.5 (10.4)
Educational level	3.6 (0.8)
WAIS-R IQ	115.5 (15.9)
Response time to angry faces (ms)	1085 (203)
Accuracy for angry faces (% correct)	89.3 (6.3)
Response time to fearful faces (ms)	1048 (218)
Accuracy for fearful faces (% correct)	97.6 (4.4)
Response time to sad faces (ms)	1185 (211)
Accuracy for sad faces (% correct)	90.6 (9.3)

Table 2. Voxel-based whole brain SPM analysis: Brain regions showing significant main effects in terms of hemodynamic responses to the presentation of emotional faces compared to neutral faces (* $p < 0.05$, FWE cluster-level corrected across the whole brain with a voxel-level cut-off of $p < 0.001$).

Brain Region	BA	Laterality	Coordinates			Cluster Size (voxels)	Z - value
			x	y	z		
Emotional faces compared to neutral faces							
Middle Occipital Gyrus/	18	R/L	38	-84	-4	147	5.94*
Inferior Occipital Gyrus	19		44	-78	-6		5.38*
Middle Occipital Gyrus	18		-24	-94	4	22	4.65*
Lingual Gyrus	18	R	10	-82	2	240	5.6*
Inferior Temporal Gyrus	37	L	-48	-66	-6	56	5.25*
Middle Frontal Gyrus	8	R/L	54	12	42	64	5.11*
			-50	8	44	4	3.29
Superior Parietal Gyrus	7	R	34	-62	54	23	4.97*
Fusiform Gyrus	19	R	24	-56	-12	49	4.81*
Cuneus	17	L	-16	-96	4	10	4.57*
Inferior Frontal Gyrus	47	R	51	20	-6	3	4.55*
Precuneus	7	R	2	-80	46	84	4.41
Amygdala	N/A	R/L	20	-2	-16	5	3.21**
Superior Temporal Gyrus/	38		-32	6	-22	332	4.29**

Amygdala	N/A		-22	0	-18		
Inferior Parietal Lobule	40	L	-50	-42	52	42	4.03
Postcentral Gyrus	2	L	-62	-22	28	13	3.65
Postcentral Gyrus	1	L	-58	-28	42	13	3.43
Inferior Frontal Gyrus	10	R	46	46	4	1	3.15

* $P < 0.05$, FWE cluster-level corrected across the whole brain with a voxel-level cut-off of $p < 0.001$.

** Survive small volume correction, $p < 0.01$, FWE cluster-level.

MNI coordinates denote the distance in mm from the anterior commissure, with positive X = right of midline, positive Y = anterior to the anterior commissure, and positive Z = dorsal to a plane containing both the anterior and the posterior commissures. Abbreviations: **R**: Right; **L**: Left; **BA**: Brodmann Area;

N/A: Not Applicable

Table 3. Mean (standard deviations) DCM endogenous parameter and modulatory estimates for all connections across all subjects and across all models.

Connection type	Mean	SD	Minimum	Maximum	Kolmogorov-Smirnov test Z-value	P- value
<i>Endogenous parameters</i>						
IOG→FG	0.130	0.185	-0.128	0.556	5.149 ¥	<0.0001**
IOG→AMY	0.067	0.108	-0.271	0.293	3.889 ¥	<0.0001**
IOG→VPFC	0.236	0.160	-0.134	0.524	8.070 ¥	<0.0001**
FG→IOG	0.002	0.039	-0.115	0.103	0.908	0.381
FG→AMY	0.002	0.017	-0.035	0.048	0.678 ¥	0.502
FG→VPFC	0.005	0.030	-0.084	0.104	1.264	0.082
AMY→IOG	0.002	0.017	-0.035	0.048	0.673 ¥	0.508
AMY→FG	0.021	0.047	-0.088	0.258	1.443	0.031*
AMY→VPFC	0.014	0.033	-0.035	0.165	1.331	0.058
VPFC→IOG	0.005	0.030	-0.084	0.104	1.264	0.082
VPFC→FG	0.042	0.079	-0.033	0.427	1.367	0.048*
VPFC→AMY	0.018	0.039	-0.030	0.182	1.535	0.018*
<i>Modulatory parameters</i>						
IOG→VPFC <i>Anger</i>	0.026	0.052	-0.026	0.286	1.935	0.001**
FG→ VPFC <i>Anger</i>	0.006	0.014	-0.006	0.082	1.686	0.007*
AMY→ VPFC <i>Anger</i>	0.003	0.008	-0.005	0.048	1.300	0.068
IOG→ VPFC <i>Fear</i>	0.011	0.051	-0.238	0.123	1.543	0.017*
FG→ VPFC <i>Fear</i>	0.003	0.010	-0.027	0.037	1.250	0.088

Connection type	Mean	SD	Minimum	Maximum	Kolmogorov-Smirnov test Z-value	P- value
AMY→ VPFC <i>Fear</i>	0.001	0.005	-0.014	0.023	1.028	0.241
IOG→ VPFC <i>Sad</i>	0.022	0.044	-0.032	0.172	1.278	0.076
FG→ VPFC <i>Sad</i>	0.004	0.010	-0.012	0.029	1.533	0.018*
AMY→ VPFC <i>Sad</i>	0.001	0.004	-0.014	0.015	1.019	0.250

* Difference significant a $p < 0.05$ uncorrected for multiple comparisons.

** Difference survives Bonferroni correction for multiple comparisons, corrected p -value=0.002.

¥ T-statistics

Figure 1

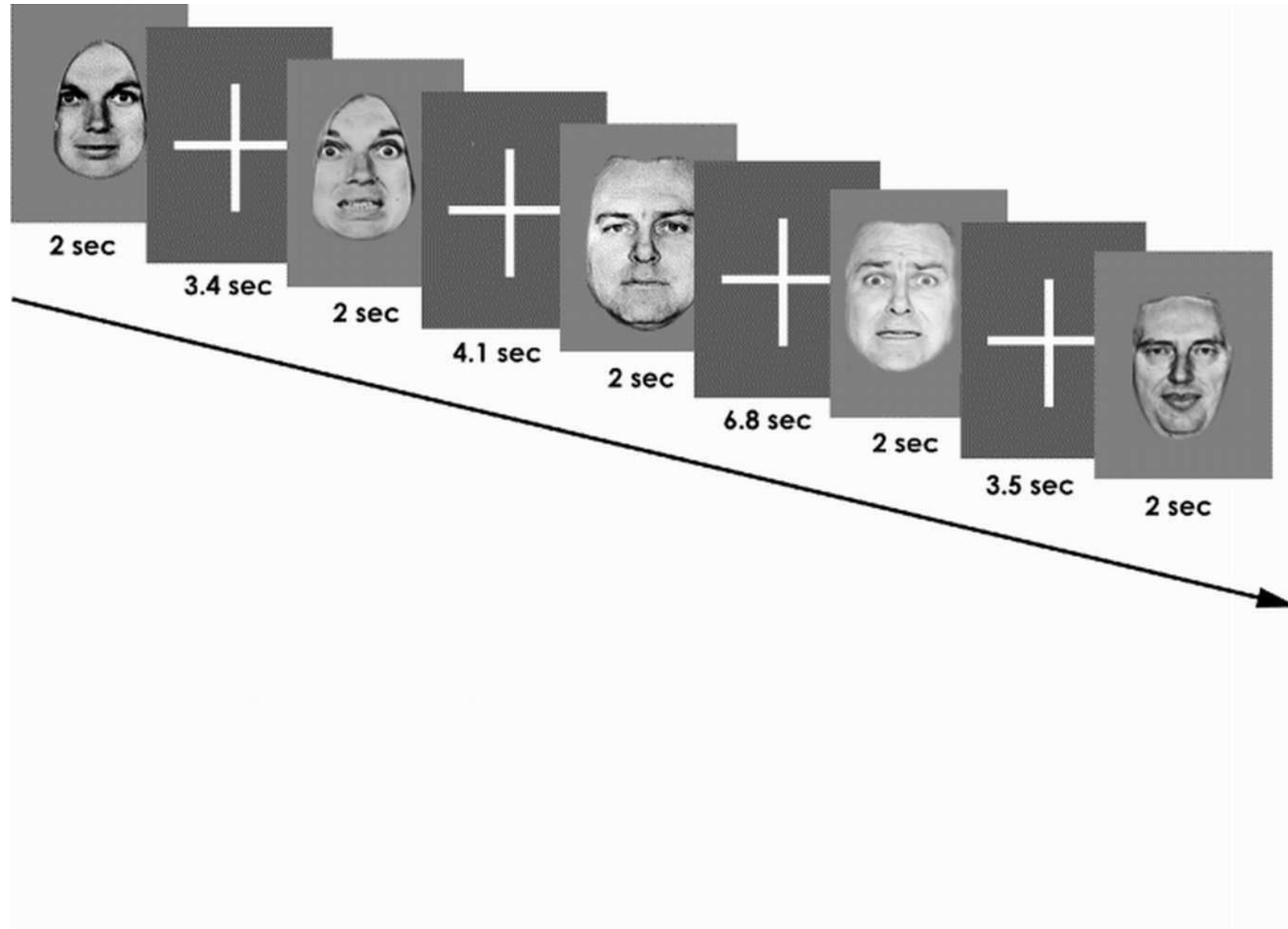


Figure 2

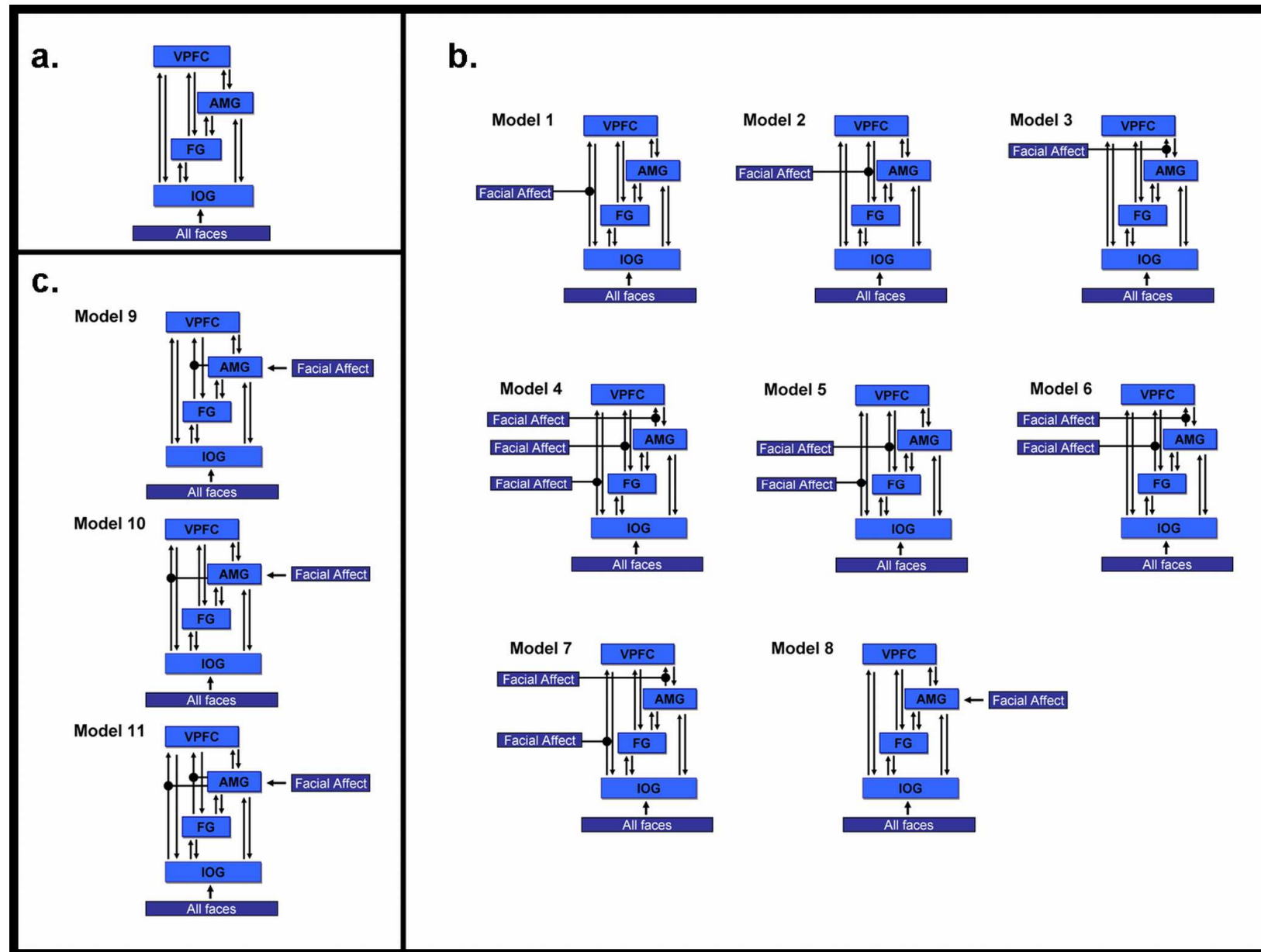


Figure 3

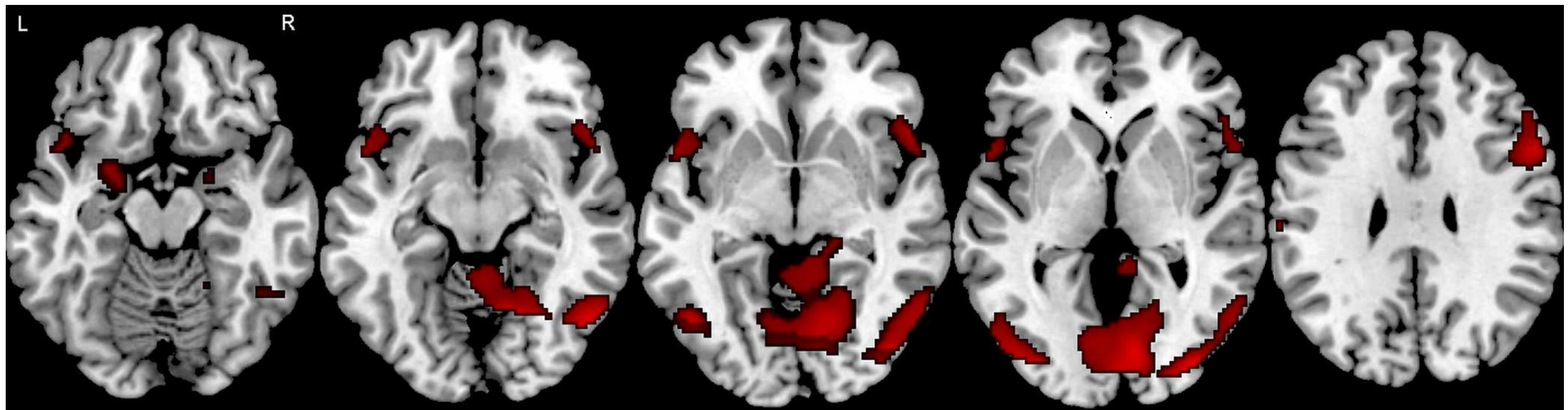


Figure 4

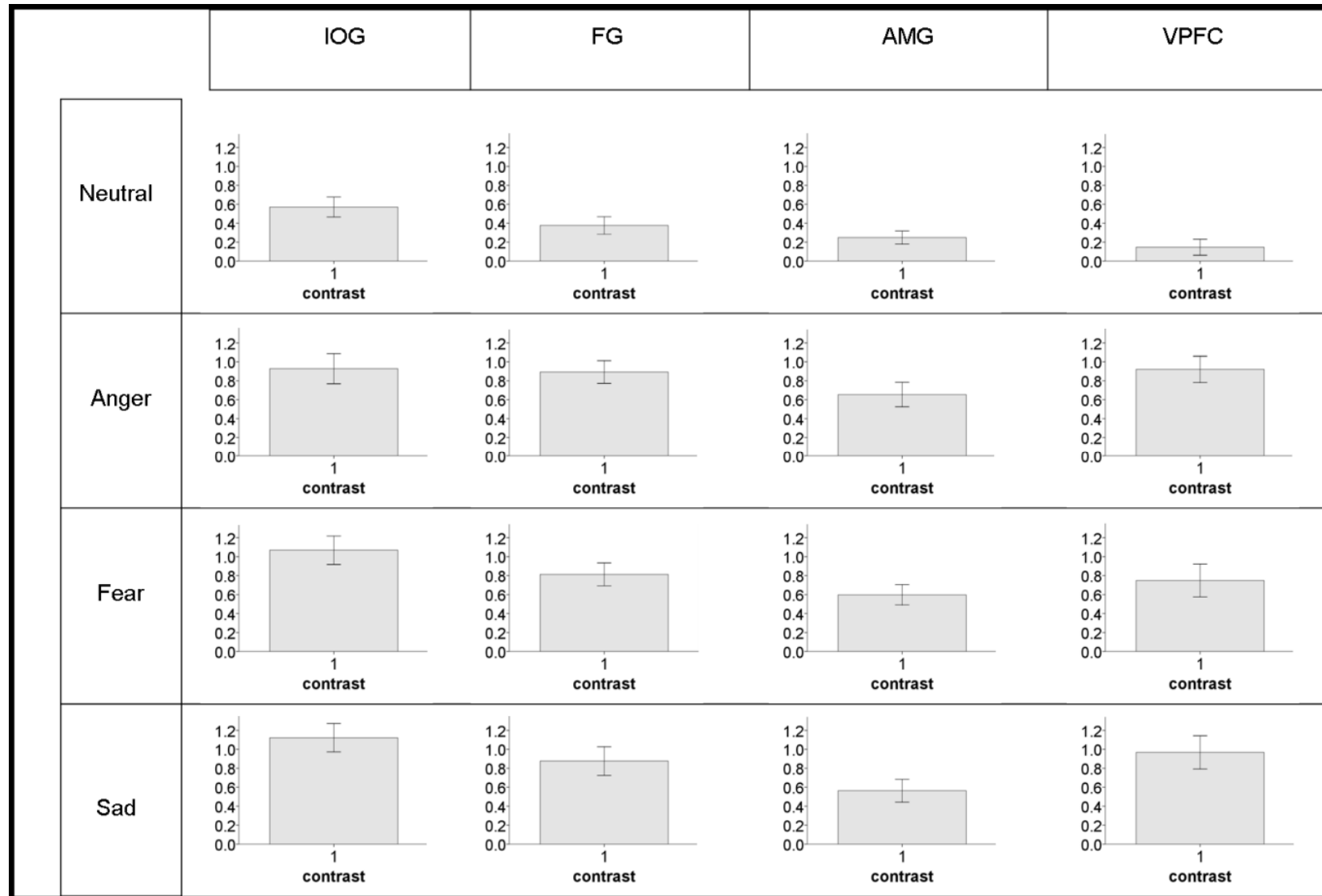


Figure 5

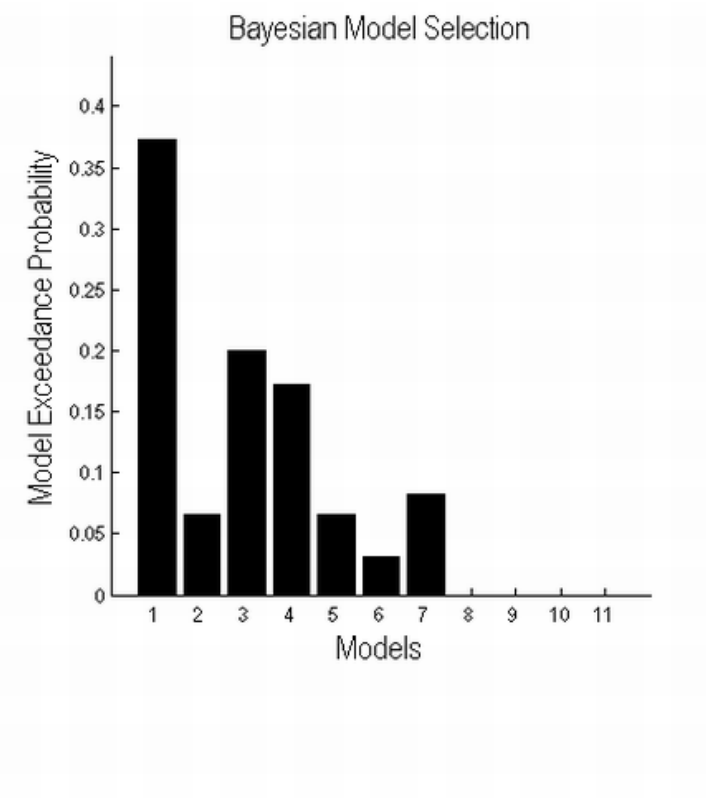
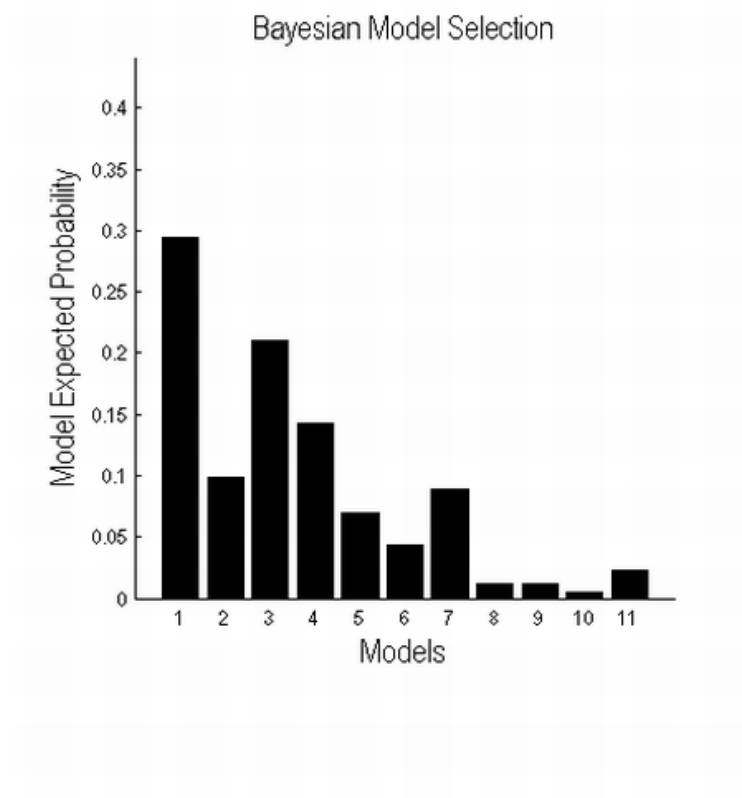


Figure 6

